## REMARKS

Restriction Requirement

In the Restriction Requirement, the Examiner requested Applicants to elect one of the following inventions:

Groups1-25 (claims 1-2 and 15) drawn to a polypeptide of SEQ ID NOs:1-25

Groups 26-50 (claims 3-6, 8 and 10-11) drawn to a nucleic acid encoding a polypeptide of SEQ ID NOs:1-25, a vector, a host cell, and a process for producing the protein.

Groups 51-75 (claim 7) drawn to a transgenic organism comprising a nucleic acid encoding a polypeptide of SEQ ID NOs:1-25.

Groups 76-100 (claim 9) drawn to an antibody to a polypeptide of SEQ ID NOs:1-25.

Groups 101-125 (claims 12-14) drawn to a method of detecting a target polynucleotide in a sample using a nucleic acid encoding a polypeptide of SEQ ID NOs:1-25.

Groups 126-150 (claim 16) drawn to a method of treatment by administering a polypeptide of SEQ ID NOs:1-25.

Groups 151-175 (claims 17, 20 and 23) drawn to a method of screening for an agonist or an antagonist of the polypeptide of SEQ ID NOs:1-25 or that alters the expression of the polynucleotide encoding the polypeptide of SEQ ID NOs:1-25.

Groups 176-200 (claims 18 and 21) drawn to an agonist or an antagonist of the polypeptide of SEQ ID NOs:1-25.

Groups 201-225 (claims 19 and 22) drawn to a method of treatment with the agonist or antagonist of the polypeptide of SEQ ID NOs:1-25.

The Examiner further stated that should on eof the Groups from 1-225 be elected, Applicanst is required to select one polypeptide (one amino acid sequence) as set forth in Table 1. Once one polypeptide sequence is selected, all other sequences will be withdrawn from consideration.

The Examiner stated that the inventions listed as Groups 1-225 do not relate to a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2 they lack the same or corresponding special technical feature for the following reasons:

The PCT rules define a special technical feature as a feature which defines a contribution

over the prior art. The first claimed invention fails to recite such a feature since any fragment of an isolated protein comprising an amino acid fragment of the polypeptide sequence set forth in SEQ ID NO:1 meets the limitations of the first invention. Furthermore, a biologically active fragment encompasses a single amino acid and any single amino acid of the 35-40 kD proteins disclosed in WO 92/05256 meets the limitations of the first invention. Since the first claimed invention lacks a special technical feature, the other claimed inventions cannot share a special technical feature with the first claimed invention.

Applicants hereby elect, with traverse, to prosecute Group 34, which includes and is drawn to Claims 3-6, 8 and 10-11, and to the nucleic acid sequence of SEQ ID NO:34 encoding the protein of amino acid sequence SEQ ID NO:9. Applicants traverse the Restriction Requirement for at least the following reasons.

The unity of invention standard ***must*** be applied in national stage applications

Section 1850 of the Manual of Patent Examining Procedure (original 8th edition, published August, 2001) (hereinafter "MPEP") provides:

> ... [W]hen the Office considers international applications ... during the national stage as a Designated or Elected Office under 35 U.S.C. 371, PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 U.S.C. 111....
>
> In applying PCT Rule 13.2 to ... national stage applications under 35 U.S.C. 371, examiners should consider for unity of invention all the claims to different categories of invention in the application and permit retention in the same application for searching and/or preliminary examination, claims to the categories which meet the requirements of PCT Rule 13.2....

*Id* at page 1800-60 to -61.

MPEP section 1893.03(d) reiterates the Examiner's obligation to apply the Unity of Invention standard PCT Rule 13.2 instead of U.S. restriction/election of species practice:

> Examiners are reminded that unity of invention (not restriction) practice is applicable ... in national stage (filed under 35 U.S.C. 371) applications.

*Id* at page 1800-149, column 1.

The present application, filed under 35 U.S.C. §371 is a national-stage application; the Examiner is therefore **required** to apply the unity of invention standard.

1. Unity of Invention is accepted between claims to polypeptides and claims to the polynucleotides which encode them

Example 17, Part 2 of Annex B to the Administrative Instructions Under the PCT provides that unity of invention is accepted between a protein and the polynucleotide that encodes it:

> *Example 17*
> Claim 1: Protein X.
> Claim 2: DNA sequence encoding protein X.
> Expression of the DNA sequence in a host results in the production of a protein which is determined by the DNA sequence. The protein and the DNA sequence exhibit corresponding special technical features. Unity between claims 1 and 2 is accepted.

Applicants submit that claims drawn to the polypeptide sequence of SEQ ID NO:9 (*i.e.*, claims 1-2 and 15 of Group 9) and claims drawn to the elected polynucleotide sequence of SEQ ID NO:34, which encodes SEQ ID NO:9 (*i.e.*, claims 3-6, 8 and 10-11 of Group 34), meet the unity of invention requirements and should be examined together.

2. Unity of invention exists with respect to dependent claims in the same claim category as the independent claim from which they depend

MPEP section 1850(A) and 1893.03(d), which recite the provisions of paragraph (c) of Part 1 (entitled "Instructions Concerning Unity of Invention") of Annex B (entitled "Unity of Invention") to the Administrative Instructions Under the PCT, provides:

**(A) Independent and Dependent Claims.**

> Unity of invention has to be considered in the first place only in relation to the independent claims in an international application and not the dependent claims. By "dependent" claim is meant a claim which contains all the features of another claim and is in the same category of claim as that other claim (the expression "category of claim" referring to the classification of claims according to the subject matter of the invention claimed for example, product, process, use or apparatus or means, etc.).
>
> (i) If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims. In particular, **it does not matter if a dependent claim itself contains a further invention**.... (Emphasis added.)

See MPEP section 1850(A) at page 1800-61. See also MPEP Appendix AI at page 53.

Accordingly, claim 9, drawn to antibodies, should also be examined together with claim 1, drawn to the polypeptides from which claim 9 depends. Moreover, claims 15, 18 and 21 all of which depend from claim 1, are directed to compositions of matter, *i.e.*, to products. Further, as discussed above, there is unity of invention among claims 1-4 and 10.

3. Unity of invention exists among all of Applicants' claims

MPEP 1850 provides:

> Unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more special technical features. The term "special technical features" is defined as meaning those technical features that define a contribution which each of the inventions considered as a whole, makes over the prior art. The determination is made based on the contents of the claims as interpreted in light of the description and drawings. Annex B also contains examples concerning unity of invention.

*Id* at page 800-61.

MPEP 1893.03(d) similarly provides:

> A group of inventions is considered linked to form a single general

> inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical features is defined as meaning those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art. For example, a corresponding technical feature is exemplified by a key defined by certain claimed structural characteristics which correspond to the claimed features of a lock to be used with the claimed key. Note also examples 1-17 of Annex B Part 2 of the PCT Administrative Instructions as amended July 1, 1992 contained in Appendix AI of the MPEP.

*Id* at page 1800-149.

In the present case, unity of invention exists among all of Applicants' claims. The sequences of the claimed polypeptides and the sequences of the claimed polynucleotides encoding those polypeptides are corresponding technical features which are common to all of Applicants claims, which serve to technically interrelate all of Applicants' claims, and which define the contribution over the prior art made by each of them. Thus all of applicants inventions related to SEQ ID NOs:9 and 34 relate to a single general inventive concept under PCT Rule 13.1, and should be examined together in a single national stage application.

4. <u>The sequences of the claimed polypeptides and the claimed polynucleotides encoding those polypeptides, are corresponding technical features that are common to all of Applicants' claims and that serve to technically interrelate them</u>

The sequences of the claimed polypeptides and corresponding polynucleotides are common to all of Applicants' claims, given that each claim refers to one or both either explicitly or implicitly, by virtue of depending from a claim which makes an explicit reference to the sequences of the claimed polypeptides or claimed polynucleotides.

Moreover, the sequences of the claimed polypeptides and corresponding polynucleotides serve to technically interrelate all of Applicants' claims. Applicants' composition of matter claims 1-7, 9-11, 15, 18 and 21) are drawn to either the polypeptides or polynucleotides themselves (1 and 2, drawn to polypeptides, and 3-4, and 10-11, drawn to polynucleotides), to

compositions of matter which comprise the polypeptides or polynucleotides as one element (claims 5-7, drawn to recombinant polynucleotides, a transformed cell or transgenic organism containing the recombinant polynucleotide, respectively, and claim 15, drawn to a pharmaceutical composition comprising the protein), or to compositions of matter wherein the sequences of the claimed polypeptides functionally limit the claimed subject matter (Claim 9, drawn to an antibody which specifically binds a polypeptide of claim 1, and claims 18 and 21 drawn, respectively to a composition comprising an agonist or an antagonist of the polypeptide of claim 1).

In Applicants' method claims 8, 12-14, 16-17, 19-20 and 22-23, the claimed polypeptides or polynucleotides serve as either the product of the claimed method (claim 8, drawn to a method of polypeptide production) and/or as a reagent for performing the method (claims 12-14, drawn to methods of detecting a polynucleotide in a sample; claims 16, 19 and 22, drawn to a method of treating or preventing a disease or condition associated with EXMAD expression; claims 17 and 20, drawn to a method of screening for an agonist or antagonist of EXMAD; and claim 23, drawn to a method for screening for a compound that alters the expression of the polynucleotide encoding EXMAD).

Therefore, the claimed polypeptide and polynucleotide sequences are corresponding technical features which are common to all of Applicants' claims, and which serve to technically interrelate them. In addition, the claimed polypeptide and polynucleotide sequences define the contribution made by each of Applicants' claims over the prior art as explained below.

5. The claimed polypeptide and polynucleotide sequences define the contribution made by each of Applicants' claims over the prior art

At page 4 of the Restriction Requirement, the Examiner argues that the claimed inventions fail to define a special technical feature that defines a contribution over the prior art because "any fragment of an isolated protein comprising an amino acid fragment of the polypeptide sequence of SEQ ID NO:1 meets the limitations of the first invention, and furthermore, that a biologically active fragment encompasses a single amino acid and any single amino acid of the 35-40 kD proteins disclosed in WO 92/05256 meets the limitations of the first

invention. Since the first claimed invention lacks a special technical feature, the other claimed inventions cannot share a special technical feature with the first claimed invention".

Applicants respectfully disagree with the Examiner's reasoning. Applicants first wish to emphasize that it is those polypeptide sequences and/or those corresponding polynucleotide sequences in their ***entire*** form which provide the "common or corresponding special technical feature" linking all of the claims to form a single general inventive concept.

Applicants respectfully point out that the full-length polypeptide and corresponding full-length polynucleotide sequences recited in Claims 1 and 11, and the claims dependent thereon, are not anticipated by any *fragments* of these sequences. Therefore, the contribution over the prior art represented by the full-length polypeptide and polynucleotide sequences is not negated by any such fragments. In addition, the Examiner's allegation that *any* single amino acid of the 35 or 40 kD proteins disclosed in WO 92/05256 constitutes a "biologically active fragment" as defined by claim 1 ignores applicants disclosure in Table 2 that SEQ ID NO:9, encoded by applicants elected polynucleotide SEQ ID NO:34, is identified as a "Leucine-Rich Repeat" protein (LLR) which are described at page 6 of the specification as functioning in protein-protein interactions. Thus no "single" amino acids from *any* proteins could anticipate such a "biologically active fragment" of SEQ ID NO:9.

In sum, the claimed polypeptide sequences and the claimed polynucleotide sequences which encode them are corresponding technical features which are common to all of Applicants claims, which serve to technically interrelate all of Applicants' claims, and which define the contribution over the prior art made by each of them. Thus, Applicants' claims are linked to form a single general inventive concept, and Applicants are therefore entitled to prosecute all of their pending claims in a single national stage application.

Applicants therefore request reconsideration of the Restriction Requirement and examination of all of claims 1-23 with respect to SEQ ID NOs:9 and 34.

Applicants reserve the right to prosecute the subject matter of non-elected claims in subsequent divisional applications.

## CONCLUSION

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

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